specifically binds to an antigen with an affinity constant of at least about $10^8\ M^{-1}$ and no greater than about four-fold that of the donor immunoglobulin, wherein the sequence of the humanized immunoglobulin heavy chain variable region framework is at least 65% identical to the sequence of the donor immunoglobulin heavy chain variable region framework and comprises at least 70 amino acid residues identical to those in the acceptor human immunoglobulin heavy chain variable region framework.

33. A vector comprising first and second polynucleotides according to claim 32.

34. First and second polynucleotides respectively encoding heavy and light chain variable regions of a humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least about $10^8\ M^{-1}$ and no greater than about four-fold that of the donor immunoglobulin, wherein the sequence of the acceptor immunoglobulin heavy chain variable region framework is a

consensus sequence of human immunoglobulin heavy chain variable region frameworks.

35. First and second polynucleotides respectively encoding heavy and light chain variable regions of a humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least about $10^8\ M^{-1}$ and no greater than about four-fold that of the donor immunoglobulin, wherein said humanized immunoglobulin heavy chain comprises one or more amino acids from the donor immunoglobulin heavy chain framework outside the Kabat and Chothia CDRs, wherein the donor amino acids substitute for corresponding amino acids in the acceptor immunoglobulin heavy chain framework, and each of these said donor amino acids:

(I) is adjacent to a CDR in the donor immunoglobulin sequence, or

(II) contains an atom within a distance of 6 ANGSTROM of a CDR in said humanized immunoglobulin.

36. First and second polynucleotides respectively encoding heavy and light chain variable regions of a humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of a least about $10^8\ M^{-1}$ and no greater than about four-fold that of the donor immunoglobulin, wherein said humanized immunoglobulin heavy chain comprises one or more amino acids from the donor immunoglobulin heavy chain framework outside the Kabat and Chothia CDRs that substitute for the corresponding amino acids in the acceptor immunoglobulin heavy chain framework, wherein each of these said donor amino acids:

(I) is adjacent to a CDR in the donor immunoglobulin sequence, or

(II) is capable of interacting with amino acids in the CDRs, or

(III) is typical at its position for human immunoglobulin sequences, and the substituted amino acid in the acceptor is rare at its position for human immunoglobulin sequences.

37. A cell line transfected with a vector according to claim 33.

38. First and second polynucleotides respectively encoding heavy and light chain variable regions of a humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant within about four-fold of that of the donor immunoglobulin, wherein the sequence of the humanized immunoglobulin heavy chain variable region framework is at least 65% identical to the sequence of the donor immunoglobulin heavy chain variable region framework and comprises at least 70 amino acid residues identical to those in the acceptor human immunoglobulin heavy chain variable region framework.

39. First and second polynucleotides respectively encoding heavy and light chain variable regions of a humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant within about four-fold of that of the donor

immunoglobulin, wherein the sequence of the acceptor immunoglobulin heavy chain variable region framework is a consensus sequence of human immunoglobulin heavy chain variable region frameworks.

40. First and second polynucleotides respectively encoding heavy and light chain variable regions of a humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen with an affinity constant within about four-fold of the donor immunoglobulin, wherein said humanized immunoglobulin heavy chain comprises one or more amino acids from the donor immunoglobulin heavy chain framework outside the Kabat and Chothia CDRs, wherein the donor amino acids substitute for corresponding amino acids in the acceptor immunoglobulin heavy chain framework, and each of these said donor amino acids:

(I) is adjacent to a CDR in the donor immunoglobulin sequence, or

(II) contains an atom within a distance of 6 ANGSTROM of a CDR in said humanized immunoglobulin.

41. A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variableregion frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least 10^7 M^{-1} and no greater than about four-fold that of the donor immunoglobulin, wherein the sequence of the humanized immunoglobulin heavy chain variable region framework is at least 65% identical to the sequence of the donor immunoglobulin heavy chain variable region framework and comprises at least 70 amino acid residues identical to an acceptor human immunoglobulin heavy chain variable region amino acid sequence.

42. A humanized immunoglobulin according to claim 41 which is an antibody comprising two light chain/heavy chain dimers.

43. A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least about 10^8 M^{-1} and no

greater than about four-fold that of the donor immunoglobulin, wherein the sequence of the acceptor immunoglobulin heavy chain variable region framework is a consensus sequence of human immunoglobulin heavy chain variable region frameworks.

44. A pharmaceutical composition comprising a humanized immunoglobulin of claim 41 in a pharmaceutically acceptable carrier.

45. A method of producing the humanized immunoglobulin of claim 41 comprising:

introducing DNA segments encoding the humanized immunoglobulin heavy and light chains into a cell; and

expressing the DNA segments in the cell to produce the humanized immunoglobulin.

46. A method of producing a humanized immunoglobulin, comprising the steps of:

(1) comparing the sequence of a donor immunoglobulin heavy chain variable region against a collection of sequences of human heavy chain variable regions;

(2) selecting a human heavy chain variable region from the collection of human heavy chain variable regions to provide an acceptor heavy chain variable region, wherein the selected

variable region framework is at least 65% identical to the donor immunoglobulin heavy chain variable region framework;

(3) synthesizing a DNA segment encoding a humanized heavy chain variable region, comprising CDRs from the donor immunoglobulin heavy chain variable region and a variable region framework from the selected acceptor heavy chain variable region;

(4) introducing the DNA segment encoding the humanized immunoglobulin heavy chain variable region and a DNA segment encoding a humanized immunoglobulin light chain variable region into a cell; and

(5) expressing the DNA segments in the cell to produce the humanized immunoglobulin.

47. A method of producing a humanized immunoglobulin, comprising the steps of:

(1) comparing the sequence of a donor immunoglobulin light chain variable region against a collection of sequences of human light chain variable regions;

(2) selecting a human light chain variable region from the collection of human light chain variable regions to provide an acceptor light chain variable region, wherein the selected

variable region framework is at least 65% identical to the donor immunoglobulin light chain variable region framework;

(3) synthesizing a DNA segment encoding a humanized light chain variable region, comprising CDRs from the donor immunoglobulin light chain variable region and a variable region framework from the selected acceptor light chain variable region;

(4) introducing the DNA segment encoding the humanized immunoglobulin light chain variable region and a DNA segment encoding a humanized immunoglobulin heavy chain variable region into a cell; and

(5) expressing the DNA segments in the cell to produce the humanized immunoglobulin.

48. A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant within about four-fold of that of the donor immunoglobulin, wherein the sequence of the acceptor immunoglobulin heavy chain variable region framework is a consensus sequence of human immunoglobulin heavy chain variable region frameworks.